

## REMARKS

### *Status of the Claims*

Upon entry of the amendment, claims 1-43 are pending.

Support for the amendment of claim 1 and new claims 40-42 can be found, for example, in paragraph 58 and the examples shown throughout the specification.

Support for new claims 43-47 is found, for example, in paragraph 127, which shows a species of macrocycle and which states that “[w]ith the synthetic methodology discussed above, macrocyclic compounds that include TIAMs can be prepared”; paragraph 84, which shows a general structure of a chelating agent that includes TIAMs; and paragraphs 108 to 126, which describe various schemes for synthesizing multidentate triamide isophthalamide ligands, abbreviated as TIAMs. In particular, Scheme 3 shows chelating agents 9A to 9I in which various types of substituents can be placed on the amide opposite the hydroxy group in the various triamide isophthalamide moieties.

Support for the amendment of claim 36 is found, for example, in paragraphs 170-177.

Support for the amendment of claims 37 and 38 is found, for example, in paragraph 260.

### *Claim Rejections under 35 USC 112*

#### **Claims 1, 2, 4, 7-10, 13-22 and 36-38**

Claims 1, 2, 4, 7-10, 13-22 and 36-38 are rejected under 35 USC 112 as allegedly indefinite for reciting “cleavable group” and “protecting group”. Applicant disagrees.

Paragraph 91 indicates that cleavable groups include “bonds that are reversible (e.g., easily hydrolyzed) or partially reversible (e.g., partially or slowly hydrolyzed).” Various conditions can induce cleavage, such as appropriate pH, ionic strength and the presence of degradative enzyme, which could include non-specific aminopeptidases, esterases, dipeptidyl carboxypeptidases, proteases of the blood clotting cascade, and the like. See ¶¶ 91 and 92. Methods for determining susceptibility of the cleavable group to degradation is also described in paragraph 95.

The term “protecting group” is well known in the art. One example textbook definition provides that a protecting group is “a functional group that can be formed reversibly and lacks the reactivity of another part of the molecule.” Fox & Whitesell, Organic Chemistry 842 (Jones and Bartlett Publishers 1994). Numerous treatises on protecting groups are known in the art, including John Frederick William McOmie,

Protective Groups in Organic Chemistry (Plenum Press 1973); James Ralph Hanson, Protecting Groups in Organic Synthesis (Sheffield Academic Press 1999); and Greene *et al.*, Protective Groups in Organic Synthesis (John Wiley & Sons 1991) as referred to in paragraph 98.

One of skill in the art would therefore be able to interpret the metes and bounds of the claims including these terms.

### **Claim 2**

Claim 2 is rejected under 35 USC 112 as allegedly indefinite for reciting “protected or unprotected reactive functional groups and non-covalent protein binding groups.” Applicant disagrees.

The term “protected” is described above. A “reactive functional group” is a commonly used term of art. For example, a functional group has been defined as “a site in a molecule at which it undergoes characteristic and selective chemical reactions” (Fox at 831). According to another definition, functional groups are “atoms or groups of atoms [that] tend to be sites of comparatively high chemical reactivity”. Vollhardt & Schore, Organic Chemistry 41 (W. H. Freeman and Co., 2d ed., 1994). Numerous examples of functional groups are described in paragraphs 35 and 97, the former of which also cites Sandler and Karo, eds. Organic Functional Group Preparations (Academic Press 1989) for further reference. The term “reactive”, as it is commonly understood, means “tending to participate readily in reactions”. The American Heritage Dictionary of the English Language (Houghton Mifflin Company, 4th ed., 2000, updated in 2009).

The term “non-covalent protein binding group” is described in paragraph 99. There, the specification points out that this term is used to describe a subset of reactive functional groups that includes moieties that interact with an intact or denatured polypeptide in an associative manner. Examples of interactions are described (e.g., hydrophobic-hydrophobic and electrostatic interactions) as are specific species (e.g., phosphate, thiophosphate, phosphonate, carboxylate, boronate, sulfate, sulfone, thiosulfate, thiosulfonate and sulfonate).

One of skill in the art would therefore be able to interpret the metes and bounds of the claims including these terms.

### **Claim 5**

Claim 5 is rejected under 35 USC 112 as allegedly indefinite for reciting “linking member” and “carrier molecules”. Applicant disagrees.

Paragraph 37 defines a linking member as a covalent chemical bond that includes at least one heteroatom, and exemplary linking members include  $-\text{C}(\text{O})\text{NH}-$ ,

-C(O)O-, -NH-, -S-, -O-, and the like. As claim 5 makes apparent, a linking member adjoins two different moieties.

According to paragraph 101, a carrier molecule is a type of molecule that, for example, can be used to target ligands (or complexes) of the invention to a specific region within the body or tissue, or to a selected species or structure *in vitro*. Examples of carrier molecules include biopolymers, poly(amino acids), polyethers, polyimines, polysaccharides, dendrimers, cyclodextrins and pharmaceutical agents according to claim 16 as filed.

One of skill in the art would therefore be able to interpret the metes and bounds of the claims including these terms.

#### **Claim 13 and 14**

Claims 13 and 14 are rejected under 35 USC 112 as allegedly indefinite since, according to the Examiner, a polymer must comprise multiple subunits, not a single subunit.

Applicant notes that nothing about claims 13 and 14 limits the claimed polymer to a single subunit. As the Examiner is aware, the transitional term “comprising” is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. MPEP 2111.03. The Examiner is also referred to *In re Baxter*, 656 F. 2d 679, 686 (CCPA 1981), in which the court, in interpreting a count reciting “[a] process for polymerizing propylene to a solid linear polymer which process comprises contacting propylene with a catalyst ....” stated that “... we are satisfied that the scope of the proposed count includes polymerizing propylene with any other monomer (copolymerization), such as ethylene, as well as homopolymerization. As long as one of the monomers in the reaction is propylene, any other monomer may be present, because the term “comprises” permits the *inclusion* of other steps, elements, or materials.”

Thus, the polymer in claims 13 and 14 is not limited to a single subunit.

#### **Claims 15-18**

Claims 15-18 are rejected under 35 USC 112 as allegedly indefinite for lack of antecedent basis for the phrase “the polymer”.

The dependency of claim 15 has been amended, and antecedent basis is present for the limitations recited therein.

#### **Claim 16**

Claim 16 is rejected under 35 USC 112 as allegedly indefinite for reciting “pharmaceutical agent”. Applicant disagrees.

The term “pharmaceutical agent” has a commonly understood meaning in the art. For example, Dorland's Medical Dictionary for Health Consumers (Saunders 2007) defines “agent” as “something capable of producing an effect”, and it defines pharmaceutical as “pertaining to pharmacy or drugs” or “a medicinal drug”. The same reference defines a drug as “a chemical substance that affects the processes of the mind or body” or “any chemical compound used in the diagnosis, treatment, or prevention of disease or other abnormal condition.” As the Examiner can appreciate, numerous examples of such substances are known in the art.

One of skill in the art would therefore be able to interpret the metes and bounds of the claims including this term.

### **Claim 16**

Claim 16 is rejected under 35 USC 112 as allegedly indefinite on the ground that “[a] broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired.”

This ground of rejection is not applicable to claim 16. The authorities cited for this ground of rejection – MPEP 2173.05(c), *Ex parte Wu*, *Ex parte Steigewald*, *Ex parte Hall* and *Ex parte Hasche* – address claims in which stated “examples and preferences” may lead to confusion over the intended scope of the claim. Examples of claim language that raise this indefiniteness issue include, according to MPEP 2173.05(c) (emphasis added), “a temperature of between 45 and 78 degrees Celsius, **preferably** between 50 and 60 degrees Celsius”; and “a predetermined quantity, **for example**, the maximum capacity.” The claim language at issue in the cited cases included, emphasis added, “material **such as** rock wool or asbestos” *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1949); “lighter hydrocarbons, **such, for example**, as the vapors or gas produced” *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949); and “normal operating conditions **such as** while in the container of a proportioner”. The Examiner herself noted that in *Ex Parte Wu*, the issue was “where broad language is followed by “**such as**” and then narrow language” (emphasis added). Thus, it is not simply the recitation of a broad range or limitation “together with” a narrow range or limitation that might render a claim indefinite, but rather, the combination of such limitations *and* the use of exemplifying language (e.g., “such as”, “for example”, “preferably”) that raises a question or doubt as to whether the feature introduced by such language is required or not. See Examiner's rejection.

The Markush group in claim 16 simply lists a number of possibilities for the moiety A, and terms such as those emphasized above are not used. Accordingly, claim 16 is not indefinite according to the reasons stated by the Examiner.

**Claim 19**

Claim 19 is rejected under 35 USC 112 as allegedly indefinite because according to the Examiner, “the only component of the chelate is the organic ligand of claim 1.” Applicant disagrees, since the claim clearly recites “A chelate **of a metal ion . . .**” In any case, in order to expedite prosecution, Applicant has amended the claim as suggested by the Examiner.

**Claims 36-38**

Claims 36-38 are rejected under 35 USC 112 as allegedly indefinite for lack of antecedent basis for the phrase “the complex”.

This term has been deleted from claims 36-38, thereby obviating their rejection.

**Claim 36**

Claim 36 is rejected under 35 USC 112 as allegedly indefinite for reciting the term “component of an ink or dye”.

This term has been deleted from the claim, thereby obviating its rejection.

**Claim 37**

Claim 37 is rejected under 35 USC 112 as allegedly indefinite for reciting the phrase “component of a substrate for the transmission and amplification of light”.

Claim 37 is now directed to a substrate for the transmission and amplification of light. Substrates are described throughout the specification. Paragraphs 150 and 151 describe the use of immobilizing substrates for carrying out enzymatic and immunological reactions in solid phase assays. Paragraphs 235 to 240 describe immobilizing compounds of the invention on any polymer or support, such as controlled pore glass, glass plates, polystyrene, avidin coated polystyrene beads, cellulose, nylon, acrylamide gel and activated dextran. Approaches for immobilizing the compounds of the invention are also described, as are various uses for the substrates in paragraph 263.

Claim 37 as amended is believed to be in compliance with 35 USC 112

**Claim 38**

Claim 38 is rejected under 35 USC 112 as allegedly indefinite for reciting organic and inorganic polymers.

The specification, paragraph 104, teaches constructs in which compounds of the invention are attached to a polymeric framework, examples of which include

polylysine, dextran, hydroxyethyl starch and the like. According to paragraph 129, examples of polymeric membranes include nylon and nitrocellulose. Paragraph 235 discloses examples including polystyrene, avidin coated polystyrene beads, cellulose and acrylamide gel. Thus, numerous examples of organic and inorganic polymers are provided by the specification.

One of skill in the art would therefore be able to interpret the metes and bounds of the claims including these terms.

***Claim Rejections under 35 USC 102***

Claims 1 and 19 are rejected under 35 USC 102(b) as allegedly anticipated by Zumstein, US Patent 2,977,332.

The claims as amended are believed to comply with 35 USC 102. Withdrawal of the rejection is respectfully requested.

***Claim Rejections for Obviousness-Type Double Patenting***

Claims 1, 2, 4, 7-10, 13-22 and 36-38 are rejected as unpatentable over claims 1-18 of copending US Patent Application 11/839,509 on the ground of obviousness-type double patenting.

Claims 1, 2, 4, 7-10, 13-22 and 36-38 are rejected as unpatentable over claims 1-8 of copending US Patent Application 12/020,470 on the ground of obviousness-type double patenting.

MPEP 804(II)(B)(1) states that the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. *In re Braat*, 937 F.2d 589 (Fed. Cir. 1991); *In re Longi*, 759 F.2d 887 (Fed. Cir. 1985).

Since the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. 103(a) rejection, the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 are employed when making an obvious-type double patenting analysis. These factual inquiries are summarized as follows: (A) Determine the scope and content of a patent claim relative to a claim in the application at issue; (B) Determine the differences between the scope and content of the patent claim as determined in (A) and the claim in the application at issue; (C) Determine the level of ordinary skill in the pertinent art; and (D) Evaluate any objective indicia of nonobviousness.

The Examiner has not performed the analysis required under *Graham*, and so has not established a *prima facie* case of obviousness of the present claims over the cited claims.

Applicant also notes that the fact that the scope of the present claims might somehow overlap with that of the cited claims is not by itself a sufficient ground for finding double patenting.

The Examiner has not shown how the pending claims are obviousness over the claims of US Patent Applications 11/839,509 and 12/020,470. Withdrawal of the rejection is respectfully requested.

***Conclusion***

Applicant believes that the claims are in condition for allowance, and early notification thereof is requested. The Examiner is invited to call the undersigned if necessary to expedite prosecution of this application.

Respectfully submitted,

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